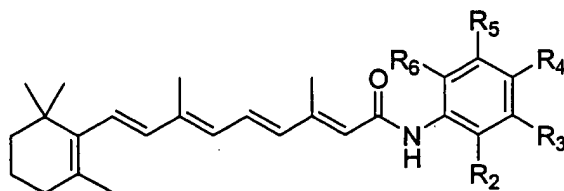


CLAIMS

What is claimed is:

1. A method of preparing an arylretinamide comprising:
 - a) reacting hexachloroacetone with a solvent-suspended resin-bound triphenylphosphine to provide a suspension comprising an activated chlorinating reagent;
 - b) reacting retinoic acid with the activated chlorinating reagent to provide retinoyl chloride;
 - c) adding pyridine and a select arylamine to the reaction mixture and stirring the resulting mixture for a time and at a temperature sufficient for the arylamine to react with the retinoyl chloride and provide the arylretinamide.
2. The method of claim 1 further comprising the step of purifying the arylretinamide from the suspension.
3. The method of claim 2 wherein purification is accomplished by treatment of the reaction mixture with solid phase reagents to remove unreacted starting materials followed by chromatography.
4. The method of claim 1 wherein step (a) is performed at a temperature ranging from about 0°C to room temperature.
5. An arylretinamide for inducing apoptosis in a cancer cell, said arylretinamide having Structure A, B, or C below:



Structure A

wherein

R_2 is H, OH, NO_2 , CH_2OH , a halide, or an alkyl comprising 1-4 carbon atoms,

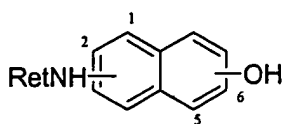
R_3 is H, OH, NO_2 , CO_2CH_3 , $\text{CO}_2\text{CH}_2\text{CH}_3$, $\text{CO}_2(\text{CH}_2)_2\text{CH}_3$, $\text{CO}_2(\text{CH}_2)_3\text{CH}_3$, CO_2H , CH_2OH , a halide, or an alkyl comprising 1-4 carbon atoms;

R_4 is H, OH, OCH_3 , OCH_2CH_3 , $\text{O}(\text{CH}_2)_2\text{CH}_3$, $\text{O}(\text{CH}_2)_3\text{CH}_3$, SO_2CH_3 , $\text{SO}_2\text{CH}_2\text{CH}_3$, $\text{SO}_2(\text{CH}_2)_2\text{CH}_3$, $\text{SO}_2(\text{CH}_2)_3\text{CH}_3$, NH_2 , NHCOCH_3 , $\text{NHCOCH}_2\text{CH}_3$, $\text{NHCO}(\text{CH}_2)_2\text{CH}_3$, $\text{NHCO}(\text{CH}_2)_3\text{CH}_3$, NHCOCF_3 , N_3 , NCS , a halide, an alkyl comprising 1-4 carbon atoms, or NHCOCH_2X , wherein X is a halide;

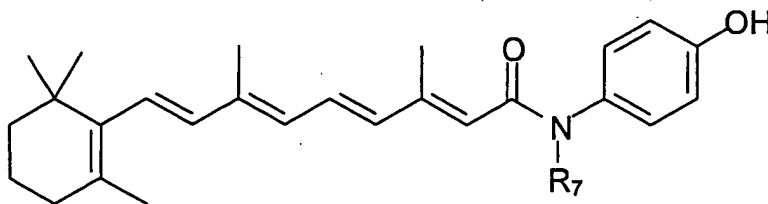
R_5 is H, NO_2 , $\text{C}(\text{CH}_3)_3$, $\text{C}(\text{CH}_2\text{CH}_3)_3$, $\text{C}((\text{CH}_2)_2\text{CH}_3)_3$, $\text{C}((\text{CH}_2)_3\text{CH}_3)_3$, CO_2CH_3 , $\text{CO}_2\text{CH}_2\text{CH}_3$, $\text{CO}_2(\text{CH}_2)_2\text{CH}_3$, $\text{CO}_2(\text{CH}_2)_3\text{CH}_3$, a halide, or an alkyl comprising 1-4 carbon atoms, and

R_6 is H, CO_2H , CO_2CH_3 , $\text{CO}_2\text{CH}_2\text{CH}_3$, $\text{CO}_2(\text{CH}_2)_2\text{CH}_3$, $\text{CO}_2(\text{CH}_2)_3\text{CH}_3$, a halide or an alkyl comprising 1-4 carbon atoms;

provided however that when R_2 , R_3 , R_4 , R_5 , and R_6 are all H, R_4 is not OH or OCH_2CH_3 ; and also provided that when R_3 , R_5 , and R_6 are all H, and R_2 is OH, R_4 is not CO_2CH_3 .

**Structure B**

wherein the OH group is at position 2,4, or 5 when the retinamido group is at linked to position 1, and the OH group is at position 3 when the retinamido group is linked to position 2.

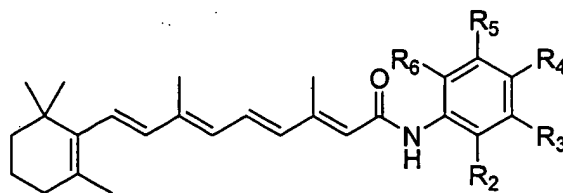


Structure C

wherein R₇ is C₁ to C₄ alkyl.

6. The arylretinamide of claim 5 wherein the arylretinamide is a halohydroxyphenyl retinamides which comprises a phenyl moiety that is optionally substituted with an alkyl group .
7. The arylretinamide of claim 6 wherein the phenyl moiety is substituted with a methyl group.
8. The arylretinamide of claim 6 wherein the halo group is an iodo group.
9. The arylretinamide of claim 5 wherein the arylretinamide is a hydroxy-alkylphenyl retinamides or hydroxy-alkoxyphenyl retinamide, wherein the alkyl groups attached to the phenyl moiety comprise from 1 to 4 carbon atoms.
10. The arylretinamide of claim 9 wherein the arylretinamide is a hydroxy-methylphenyl or hydroxy-methoxyphenyl retinamide.
11. The arylretinamide of claim 5 is a hydroxy-nitrophenyl retinamides or alkylsulfonyl-hydroxy retinamides.
12. The arylretinamide of claim 11 wherein the arylretinamide is an ethylsulfonyl-hydroxy, retinamides.
13. The arylretinamide of claim 5 wherein the arylretinamide is a hydroxy-naphthylphenyl retinamide.

14. The arylretinamide of claim 5 wherein the arylretinamide is an N-alkyl(hydroxyphenyl)retinamides.
15. The arylretinamide of claim 5 wherein the arylretinamide is an aminophenyl retinamides.
16. The arylretinamide of claim 5 wherein the arylretinamide is an alkylhydroxyphenyl retinamides.
17. The arylretinamide of claim 5 wherein the arylretinamide is a carboxy-hydroxyphenyl retinamides selected from the group consisting of *N*-(2'-hydroxy-3'-carboxymethylphenyl)retinamide, *N*-(2'-hydroxy-3'-carboxyphenyl)retinamide, *N*-(2'-hydroxy-6'-carboxymethylphenyl)retinamide, *N*-(2'-hydroxy-6'-carboxyphenyl)retinamide, *N*-(3'-hydroxy-4'-carboxymethylphenyl)retinamide, *N*-(3'-hydroxy-4'-carboxyphenyl)retinamide, *N*-(2'-hydroxy-5'-carboxymethylphenyl)retinamide, *N*-(2'-hydroxy-4'-carboxyphenyl)retinamide, *N*-(4'-hydroxy-3'-carboxymethylphenyl)retinamide, and *N*-(4'-hydroxy-3'-carboxyphenyl)retinamide.
18. An arylretinamide having Structure A below



Structure A

wherein

R₂ is H, OH, NO₂, CH₂ OH, a halide, or an alkyl comprising 1-4 carbon atoms,

R_3 is H, OH, NO_2 , CO_2CH_3 , $\text{CO}_2\text{CH}_2\text{CH}_3$, $\text{CO}_2(\text{CH}_2)_2\text{CH}_3$, $\text{CO}_2(\text{CH}_2)_3\text{CH}_3$, CO_2H , CH_2OH , a halide, or an alkyl comprising 1-4 carbon atoms;

R_4 is H, OH, OCH_3 , OCH_2CH_3 , $\text{O}(\text{CH}_2)_2\text{CH}_3$, $\text{O}(\text{CH}_2)_3\text{CH}_3$, SO_2CH_3 , $\text{SO}_2\text{CH}_2\text{CH}_3$, $\text{SO}_2(\text{CH}_2)_2\text{CH}_3$, $\text{SO}_2(\text{CH}_2)_3\text{CH}_3$, NH_2 , NHCOCH_3 , $\text{NHCOCH}_2\text{CH}_3$, $\text{NHCO}(\text{CH}_2)_2\text{CH}_3$, $\text{NHCO}(\text{CH}_2)_3\text{CH}_3$, NHCOCF_3 , N_3 , NCS , a halide, an alkyl comprising 1-4 carbon atoms, or NHCOCH_2X , wherein X is a halide;

R_5 is H, NO_2 , $\text{C}(\text{CH}_3)_3$, $\text{C}(\text{CH}_2\text{CH}_3)_3$, $\text{C}((\text{CH}_2)_2\text{CH}_3)_3$, $\text{C}((\text{CH}_2)_3\text{CH}_3)_3$, CO_2CH_3 , $\text{CO}_2\text{CH}_2\text{CH}_3$, $\text{CO}_2(\text{CH}_2)_2\text{CH}_3$, $\text{CO}_2(\text{CH}_2)_3\text{CH}_3$, a halide, or an alkyl comprising 1-4 carbon atoms, and

R_6 is H, CO_2H , CO_2CH_3 , $\text{CO}_2\text{CH}_2\text{CH}_3$, $\text{CO}_2(\text{CH}_2)_2\text{CH}_3$, $\text{CO}_2(\text{CH}_2)_3\text{CH}_3$, a halide, or an alkyl comprising 1-4 carbon atoms;

provided that when R_2 , R_3 , R_4 , R_5 , and R_6 are all H, R_4 is not OH, OCH_3 , OCH_2CH_3 , or $\text{O}(\text{CH}_2)_2\text{CH}_3$; and also

provided that when R_3 , R_5 , and R_6 are all H, and R_2 is OH, R_4 is not CO_2CH_3 or $\text{CO}_2\text{CH}_2\text{CH}_3$.

19. A method of inducing apoptosis in a cancer cell comprising contacting the cancer cell with an arylretinamide of claim 1.

20. A method of treating cancer in a subject in need of said treatment, comprising administering one or more arylretinamides of claim 1 to the subject.

21. The method of claim 20 wherein said method further comprises administering calcium glucarate to the subject.